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Factors ınfluencing mortality after cardiopulmonary resuscitation; never give up!

After cardio-pulmonary resuscitation

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Abstract

Aim: The study aims to evaluate the prognostic factors affecting mortality and neurological recovery in patients with restored circulation in in-hospital cardiac arrest (IHCA).

Material and Methods: For this retrospective study, patients who survived after cardiac arrest and followed up in the intensive care unit of our hospital between 2021 and 2023 were investigated. Sixty-one patients with in-hospital cardiac arrest were included in the study. Laboratory data and epicrises of the patients were analysed. Demographic characteristics, cardiopulmonary resuscitation (CPR) duration, mechanical ventilation (MV) duration, the intensive care unit length of stay, mortality, cerebral performance category (CPC) scores, tracheotomy and percutaneous endoscopic gastrostomy (PEG) status, Acute Physiology and Chronic Health Evaluation (APACHE) II score, Glasgow coma scale (GCS) were recorded. Patients who survived were classified as GL and those who died were classified as GM.

Results: In the current study, 22 patients were discharged from the intensive care unit. Potassium and N-terminal pro-brain natriuretic peptides were found to be predictors of mortality (p=0.006, p=.0.025). Mechanical ventilation duration, MCV, gamma glutamyl transpeptidase (GGT), CPR duration, tracheotomy and PEG status were positively correlated with CPC score (p=0.011, p=0.017, p=0.013, p=0.007, p=0.007, p=0.000, p=0.000). In GM, lactate, urea, creatinine, NT-pro-BNP and potassium values were statistically significantly higher (p=0.022, p=0.016, p=0.003, p<0.001, p=0.008, respectively).

Discussion: NT-proBNP and potassium were found to be predictors of mortality in patients with return of spontaneous circulation after IHCA. In addition, a positive correlation was found between CPR duration and CPC score. We suggested that these parameters could be included in prognostic scoring systems.

Keywords
Cardiac Arrest, Cardio-Pulmonary Resuscitation, Mortality

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This study was approved by the Ethics Committee of Giresun University Training Research Hospital (Date: 2023-12-04, No: 26)

Introduction

The follow-up and management of patients after cardiac arrest is one of the most challenging situations faced by physicians and paramedics. In particular, there is controversy about which of these patients have a good prognosis. Whether or not patients should be accepted as Do- Not- Resuscitate (DNR) after cardiac arrest can be a problem in terms of ethics, culture and even belief. Some studies have shown that there is no significant difference in mortality between in-hospital cardiac arrest (IHCA) and out-of-hospital cardiac arrest (OHCA). However, patients with IHCA are more fortunate to receive basic and advanced life support than patients with OHCA. Because they can access intervention in a shorter time.

In studies, survival after IHCA ranges between 15-20% and almost half of these patients have good cerebral performance scores, meaning that they are neurologically intact or have mild neurological deficits [1-4]. In order to improve survival and neurological status in IHCA patients, it is necessary to determine prognostic factors. Many studies have published models to predict prognostic factors after resuscitation in IHCA patients. PAM, PAR, and GO-FAR are the most important ones. The most acceptable of these models is GO-FAR [5]. These models, which mostly focus on the comorbidities of the patients before the arrest, do not include the characteristics during or after admission to the intensive care ünit (ICU).

The most common cause of cardiac arrest is cardiac diseases with 50-60%, followed by respiratory failure with 15-40% [6-8]. In our study, we excluded coronary intensive care unit patients and patients with OHCA. The reason for excluding coronary ICU patients was to rule out patients with cardiovascular causes. Unlike other studies, we evaluated the mortality and cerebral performance category (CPC) score of patients with IHCA who were followed up in the ICU by adding laboratory parameters, mechanical ventilator and ICU length of stay. Our aim was to evaluate the probability of survival in these patients and to determine the determinants of good prognosis. Thus, we targeted to enable physicians to exhibit more scientific approaches in terms of performance orientations and informing patients' relatives about death and survival.

Material and Methods

Inclusion criteria

A retrospective review of 3956 patients who were admitted to the intensive care unit of our hospital between January 2021 and December 2023 was performed. We identified 196 patients with return of spontaneous circulation (ROSC) after cardiopulmonary resuscitation (CPR). Rhythm on the monitor and manual pulse control were considered the gold standard for ROSC decision. We excluded 135 patients with OHCA or followed up in coronary ICU (Figure 1). We searched the data of 61 patients with in-hospital cardiac arrests from the hospital information system and patient files. Patients whose blood gas, haemogram, biochemistry, procalcitonin and NT-pro-BNP levels were measured within the first two hours after ROCS were included in the study.

Patients who survived were classified as GL and those who died were classified as GM.

Analysed data

Age, gender, comorbidities (Diabetes mellitus, hypertension, congestive heart failure, neurological disease, pulmonary dısease, acute renal faılure, chronic renal failure) duration of CPR, duration of mechanical ventilation, duration of intensive care unit stay, tracheostomy and percutaneous endoscopıc gastrostomy (PEG), Acute Pysiology and Chronic Health Evaluation II (APACHE II), Glasgow Coma Scale (GCS) were recorded. Blood gas pH, PaO2, PaCO2, HCO3-, BE, lactate values were recorded. Glucose, urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT), gamma glutamyl transpeptidase (GGT), lactate dehydrogenase (LDH), alkaline phosphatase (ALP), troponin, procalcitonin, N-terminal pro-brain natriuretic peptide (NT-pro-BNP), C-reactive protein (CRP), albumin, potassium, calcium, lymphocyte, neutrophil, red blood cell (RBC), (WBC), haemoglobin (Hb), haematocrit (Htc), platelet, mean corpuscular volume (MCV) values and mortality status were recorded.

Neurological evaluation

Neurological outcomes were assessed using the CPC scale, which evaluates brain recovery functionally and cognitively [9]. The CPC scale is a 5-point scale; 1 good brain performance, 2 moderate neurological defect, 3 severe cerebral disability, 4 coma or vegetative state, 5 brain death. A favourable neurological outcome was defined as a CPC score of 1 or 2 at discharge, and CPC 3 and above was considered a poor neurological outcome.

Statistical Analysis

Statistical analyses were performed with IBM SPSS v23. Normality analysis of the data was performed with Shapiro Wilk test. The comparison of normally distributed data was performed with independent sample t-test, and the comparison of non-normally distributed data was performed with Mann Whitney U test. A comparison of qualitative data was performed with Pearson Chi-square test. Logistic regression analysis was used to analyze the factors affecting survival. The relationship between CPC score and parameters was analyzed by Pearson correlation analysis. Data are presented as n (%) and mean (95% CI). Statistical significance was accepted as $p<0.05$.

Ethical Approval

This study was approved by the Ethics Committee of Giresun University Training Research Hospital (Date: 2023-12-04, No: 26)

Results

We retrospectively reviewed 3956 patients admitted to the anaesthesia intensive care unit between January 2021 and December 2023. We identified 196 patients with ROSC, of whom 135 patients (incomplete data set, OHCA or coronary ICU) were excluded. This study included 61 IHCA patients with a complete data set within the first 2 hours after ROSC. Thirty-nine patients died during intensive care unit follow-up. Twenty-two patients were discharged. At the time of discharge, six patients had a CPC score of 1 and two patients had a CPC score of 2.

Patient Characteristics

The mean age of the surviving patients was 66.7 years, and

73.3 years of the patients who died. There was no statistically significant difference between the two groups (p=0.183) (Table 1). MV duration was 42.8 days in GL and 15.6 days in GM. The duration of ICU stay was 48 days in GL and 16 days in GM. The duration of MV and ICU stay was statistically significantly higher in GL (p=0.006, p=0.001). CPR duration, APACHE II, expected mortality and GCS were not different between the two groups (p>0.05) (Table 1).

The number of male patients was higher in both groups, but there was no significant difference in terms of gender (Fig.1). When the comorbidities of the patients were analysed, there was no difference between the two groups in terms of DM, HT, congestive heart failure, neurological disease, acute and chronic renal failure and lung disease (p>0.05) (Table 2). The proportion of patients with tracheotomy and PEG was statistically significantly higher in GL (p=0.004, p<0.001) (Figure 2).

Table 1. Intra-hospital outcome after IHCA

	GL (n=22)	GM (n=39)	p
Age	66,7 (59,2 - 74,2)	73,3 (68,3 - 78,3)	0,183
MV Duration	42,8 (22,9 - 62,6)	15,6 (8,9 - 22,4)	0,006
APACHE II	18,6 (14,7 - 22,6)	23,4 (19,7 - 27)	0,138
PDR	34,2 (23,7 - 44,7)	47,1 (37 - 57,1)	0,158
GKS	6 (4 - 7)	6 (5 - 7)	0,841
pH	7,34 (7,28 - 7,41)	7,27 (7,22 - 7,33)	0,1
PaO$_2$ (mmHg)	136 (89 - 183)	126 (90 - 161)	0,543
paCO$_2$ (mmHg)	42 (37 - 48)	48 (43 - 53)	0,092
HCO$_{3-}$ (mEq/L)	22,7 (20,1 - 25,3)	21,1 (18,7 - 23,5)	0,229
BE	-2,4 (-5,7 - 0,9)	-4,2 (-7,3 - -1,1)	0,314
Laktat(mmol/L)	3,3 (2 - 4,6)	5,6 (4,2 - 7)	0,022
Lenfosit (%)	10,18 (7,01 - 13,34)	12,45 (9,25 - 15,65)	0,444
Nötrofil (%)	83,96 (80,47 - 87,46)	82,38 (79,11 - 85,64)	0,68
RBC (milyon/µL)	3,82 (3,39 - 4,25)	3,76 (3,53 - 3,99)	0,881
WBC(/mcL)	13,26 (10,47 - 16,06)	14,64 (12,17 - 17,12)	0,599
Hemoglobin (gr/dL)	11,7 (10,5 - 12,8)	10,9 (10,2 - 11,6)	0,404
Hematocrit(%)	35,7 (32,4 - 39)	34,5 (32,3 - 36,8)	0,702
Platelet (10^9/L)	218 (177 - 259)	210 (177 - 243)	0,548
MCV(fL)	95,3 (91,3 - 99,2)	91,4 (89 - 93,8)	0,11
Glucose (mg/dL)	176 (140 - 211)	216 (178 - 253)	0,108
AST(U/L)	86 (53 - 120)	316 (132 - 500)	0,359
ALT(U/L)	65 (43 - 86)	201 (79 - 324)	0,735
GGT (U/L)	80 (46 - 114)	78 (56 - 100)	0,775
LDH (U/L)	366 (298 - 435)	764 (441 - 1086)	0,069
ALP (U/L)	101 (78 - 123)	93 (82 - 103)	0,764
Urea (mg/dL)	70,1 (50,6 - 89,6)	99,6 (82 - 117,2)	0,016
Creatinine (mg/dL)	1,16 (0,94 - 1,38)	2,12 (1,63 - 2,61)	0,003
Troponin I	0,483 (0,137 - 0,829)	0,981 (0,372 - 1,589)	0,48
Procalcitonin(µg/l)	6,34 (0,4 - 12,27)	4,85 (1,89 - 7,81)	0,62
NT-pro-BNP(pg/ml)	3362 (586 - 6138)	16388 (12276 - 20499)	<0,001
CRP (mg/dL)	86,78 (44,31 - 129,25)	58,91 (34,66 - 83,15)	0,462
Albumin (g/Dl)	32,45 (29,5 - 35,4)	32,43 (30,4 - 34,47)	0,822
potassium(mEq/L)	4 (3,7 - 4,2)	4,5 (4,3 - 4,8)	0,008
Calcium (mg/dL)	8,4 (8,1 - 8,7)	8,4 (8,2 - 8,7)	0,775
ICU LOS	48 (22 - 75)	16 (9 - 23)	0,001
CPR duratıon (minute)	19,68 (14,19 - 25,17)	21,33 (16,67 - 26)	0,795

MV: Mechanical ventilation, APACHE: Acute Physiology and Chronic Health Evaluation, PDR: Predicted Death Rate GCS: Glasgow Coma Scale, RBC:Red blood cell, WBC:White blood cell, MCV:Mean corpusculer volume, AST= Aspartate aminotransferase, ALT= Alanine aminotransferase, GGT: Gamma Glutamyl Transferase, LDH: Lactate dehydrogenase, ALP: Alkaline phosphatase, NT-pro-BNP: N-terminal pro-brain natriuretic peptide, CRP: C-reactive protein, ICU LOS: Intensive care unit long stay, CPR: Cardiopulmonary resuscitation,

Laboratory Results

The median value of lactate was 3.3 mmol/L in GL and 5.6 mmol/L in GM. The median value of urea was 70.1mg/dL in GL and 99.6mg/dL in GM. Creatinine was 1.16 mg/dL in GL and 2.12 mg/dL in GM Potassium was 4 mEq/L in GL and 4.5 mEq/L in GM Pro- BNP was 3362 pg/ml in GL, 16388 pg/ml in GM. In GM, lactate, urea, creatinine, pro-BNP and potassium values were statistically significantly higher (p=0.022, p=0.016, p=0.003, p<0.001, p=0.008, respectively) (Table 1).

There was no significant difference between the groups in pH, pO2, pCO2, HCO3-, BE, lymphocyte, neutrophil, RBC,

Table 2. Factors affecting the CPC score after IHCA

	CPC	
	r	p
Age	0,016	0,945
Sex	-0,016	0,945
MV duration	0,53	0,011
APACHE II	0,228	0,308
PDR	0,223	0,319
GCS	-0,148	0,512
pH	0,352	0,108
PaO$_2$ (mmHg)	-0,031	0,891
PaCO$_2$ (mmHg)	-0,092	0,683
HCO$_{3-}$ (mEq/L)	0,284	0,2
BE	0,322	0,145
Lactate(mmol/L)	-0,288	0,193
Lenfosit (%)	-0,327	0,137
Neutrophil (%)	0,402	0,064
RBC (milyon/µL)	-0,255	0,253
WBC (/mcL)	0,008	0,971
Hemoglobin (gr/dL)	-0,18	0,424
Hematocrit (%)	-0,136	0,545
Platelet (10^9/L)	-0,178	0,427
MCV (fL)	0,502	0,017
Glucose (mg/dL)	-0,415	0,055
AST(U/L)	0,267	0,23
ALT(U/L)	0,275	0,215
GGT (U/L)	0,519	0,013
LDH (U/L)	0,189	0,401
ALP (U/L)	0,278	0,21
Urea (mg/dL)	0,046	0,839
Creatinine (mg/dL)	-0,157	0,484
Troponin I	0,078	0,729
Procalcitonin(µg/l)	0,098	0,666
NT-pro-BNP(pg/ml)	-0,049	0,827
CRP (mg/dL)	-0,14	0,535
Albumin (g/Dl)	-0,128	0,57
potassium(mEq/L)	-0,183	0,416
Calcium (mg/dL)	-0,403	0,063
ICU LOS	0,29	0,191
CPR duratıon (minute)	0,558	0,007
Tracheotomy	0,723	0
PEG	0,756	0

MV: Mechanical ventilation, APACHE: Acute Pysiology and Chronic Health Evaluation, PDR: Predicted Death Rate GCS: Glasgow Coma Scale, RBC:Red blood cell, WBC:White blood cell, MCV:Mean corpusculer volüme, AST= Aspartate aminotransferase, ALT= Alanine aminotransferase, GGT: Gamma Glutamyl Transferase, LDH: Lactate dehydrogenase, ALP: Alkaline phosphatase, NT-pro-BNP: N-terminal pro-brain natriuretic peptide, CRP: C-reactive protein, ICU LOS: Intensive care unit long stay, CPR: Cardiopulmonary resuscitation, PEG: Percutaneous endoscopıc gastrostomy

Table 3. Independent predictors affecting mortality as a result of univariate and multivariate analysis.

	Univarient Logistic Regression		Multivarient Logistic Regression	
	OR (95% CI)	p	OR (95% CI)	p
MV duration	0,970 (0,947 - 0,993)	0,012	0,997 (0,950 - 1,046)	0,892
Lactate (mmol/L)	1,190 (1,008 - 1,404)	0,04	0,930 (0,705 - 1,226)	0,605
Urea (mg/dL)	1,013 (1,001 - 1,026)	0,041	1,003 (0,976 - 1,030)	0,85
Creatinine (mg/dL)	3,349 (1,354 - 8,287)	0,009	0,882 (0,211 - 3,692)	0,864
NT-Pro-BNP (pg/ml)	1,000 (1,000 - 1,000)	0,003	1,000 (1,000 - 1,000)	0,006
Potassıum (mEq/L)	2,506 (1,197 - 5,246)	0,015	5,730 (1,247 - 26,324)	0,025
ICU LOS	0,968 (0,943 - 0,994)	0,017	0,930 (0,848 - 1,020)	0,122
Trakeotomy	0,197 (0,064 - 0,608)	0,005	54,680 (0,356 - 8407,648)	0,119
PEG	0,079 (0,021 - 0,302)	<0,001	0,012 (0,000 - 0,728)	0,035

MV: Mecanic ventilation, NT-pro-BNP: N-terminal pro-brain natriuretic peptide, ICU LOS: Intensıve care unıt length of stay, PEG: Percutaneous endoscopıc gastrostomy

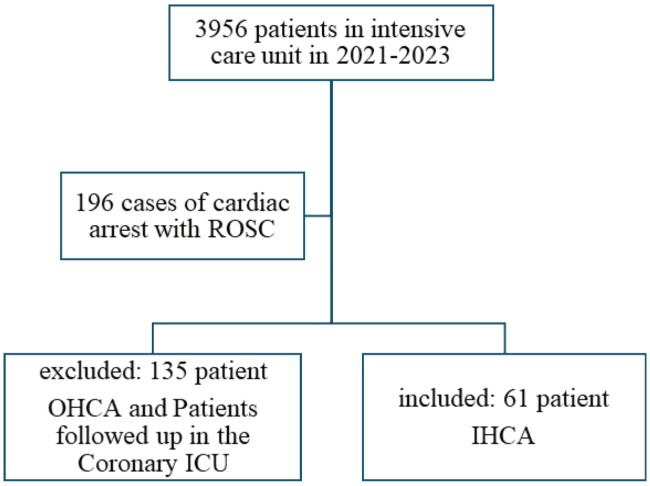
3956 patients in intensive care unit in 2021-2023
196 cases of cardiac arrest with ROSC
excluded: 135 patient OHCA and Patients followed up in the Coronary ICU
included: 61 patient IHCA

Figure 1. Flow chart of the study design. IHCA = In-hospital cardiac arrest, OHCA = Out-of-hospital cardiac arrest, ROSC = Return of spontaneous circulation, ICU = Intensive Care Unit

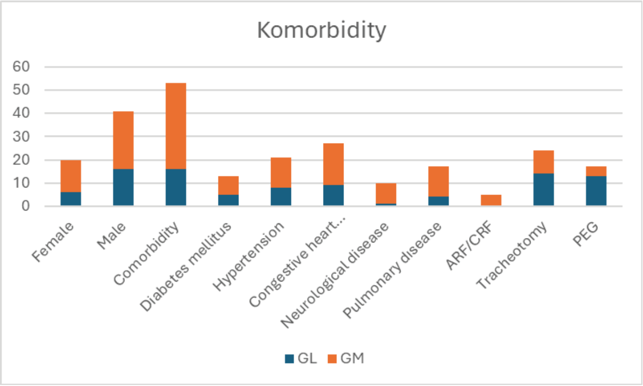

Figure 2. Demographic characteristics of patient ARF: Acute renal faılure, CRF: chronic renal failure, PEG: Percutaneous endoscopıc gastrostomy

WBC, haemoglobin, haemotocrit, platelet, MCV, glucose, AST, ALT, GGT, LDH, ALP, troponin, procalcitonin, CRP, albumin and calcium values (Table 1).

Neurological evaluation and factors affecting CPC score and mortality

Six patients had a CPC score of 1 at discharge. Two patients had a CPC score of 2. In the correlation analysis, the effects of the characteristics of the surviving patients on the cerebral performance category (CPC) score were analysed (Table 2). A positive correlation was found between MCV, GGT, MV duration, CPR duration, tracheotomy and PEG with CPC score (Table 2). Before discharge from the ICU, 63.9% of patients with ROCS died. When the relationship between the independent variables and mortality was analysed by univariate and multivariate logistic regression analysis, a positive correlation was found between NT-pro-BNP and potassium with mortality and a negative correlation with PEG (Table 3).

Discussion

The possibility of survival after CPR and discharge with a good neurological outcome (CPC score;1 or 2) confronts physicians with the choice of which patients to resuscitate and which patients to accept as DNR. Patients after CPR are generally considered to have a low likelihood of survival during follow-up and the decision to DNR may be made earlier than in the general population. Therefore, effective parameters are needed to predict mortality in this patient population. However, it is important to remember that no parameter or scoring system alone can be effective in making this decision. In this study, we have examined survival and discharge with a good CPC score in a group of patients who were followed up in the ICU after CPR. In 64% of the patients, death occurred before they were discharged from the intensive care unit. NT-pro-BNP and potassium elevation were directly correlated with mortality. Of the survivors, 36.4% were discharged with a good neurological outcome. The CPC score also increased as the duration of CPR, MCV and GGT increased.

IHCA is a common and difficult-to-treat condition. Previous studies and meta-analyses have identified groups with high and low survival rates after IHCA and reported that advanced age, malignancy, impaired renal function and dependent functional status are associated with mortality. Survival has been reported to be higher in patients with cardiovascular diagnosis [4, 5, 9]. Survival rate in IHCA varies between 15-25% [4, 9-11]. In our study, 36% of patients with ROCS survived. We found a higher survival rate compared to other studies.Age has been found to be a risk factor for mortality in many studies [4, 5, 12]. In our study, although the mean age was higher in the mortality group, no significant difference was found. Male gender has been found as a prognostic factor for mortality in some studies [13]. In this study, male gender was predominant in both groups, but no difference was found between the groups.

Considering the comorbidities of the patients, some studies have reported that chronic obstructive pulmonary disease, cirrhotic liver disease, CRF and HF worsen survival [10, 14-17]. In our study, no significant difference was found between the two groups in terms of comorbidity. However, it was observed that patients with impaired renal function had a more mortal course. In patients with ROCS, urea creatinine and potassium levels in blood samples taken within 2 hours were significantly higher in the mortality group. In addition, potassium elevation was determined as a predictive factor for mortality in the multivariation analysis.

NT-pro-BNP is secreted by the heart and vessels in response to myocardial stretch and is used in the diagnosis of heart failure [18]. Satyan et al [19] reported that NT-pro-BNP is associated with left ventricular systolic dysfunction and is a stronger predictor of mortality than troponin-t level in haemodialysis patients. In the studies, diagnosed heart failure is included among the comorbidities affecting mortality after CPR. In our study, 44.2% of patients with ROCS were previously diagnosed with heart failure. NT-pro-BNP was significantly higher in the mortal group. In the multivariate analysis, NT-pro-BNP was found to be a predictor of mortality independent of other factors.

Lactate is used as an important indicator of perfusion. After cardiac arrest, lactate and pH values may change during the period of no blood flow. Increased lactate levels have been found to be associated with mortality. In our study, similarly, lactate level was significantly higher in the mortality group [20, 21]. PEG and tracheotomy status was higher in surviving patients. We think that this is due to the fact that the need for these interventions arises more in patients who survive for a long time.

The CPC score is used to assess functional outcomes in patients after cardiac arrest [22]. It has been shown to have good validity and reliability [23]. In previous studies, more than half of the patients who survived after IHCA were intact or had mild neurological deficits at discharge [3, 4]. In our study, 36.4% of the surviving patients were discharged from the ICU with a CPC score of 1 or 2. Undoubtedly, the level of hypoxia has an effect on good neurological outcomes. Therefore, CPR efficacy and duration are determinants of hypoxia. However, there is not much information about the neurological predictive value of CPR duration. Rohlin et al. Rohlin et al. reported that the chance of 30-day survival decreased markedly as the duration of CPR increased [24]. While neurological conditions are the major cause of death in OHCA patients, this ratio is about one in four in IHCA. In IHCA, mortality is mostly determined by multiorgan failure[25]. Similarly, in our study, increased CPR time was not associated with mortality in IHCA cases, whereas there was a moderate positive correlation with CPC score. In addition, CPC score increased as MV duration, tracheotomy and PEG status increased. However, since we could not evaluate these parameters at baseline, we think that their value as predictors is limited. It may be considered that prolonged MV duration during clinical follow-up may contribute to decision making.

Scoring systems such as Pre-arrest Morbidity Score (PAM - Score), Prognosis After Resuscitation Score (PAR - Score), Good Outcome Following Attempted Resuscitation Score (GOFAR - Score) are scoring systems developed to evaluate survival and mortality after resuscitation. In our study, urea, creatinine, potassium and NT-pro-BNP were found to be higher in the mortal group. NT-pro-BNP and potassium were found to be independent predictors of mortality. We think that potassium and NT-pro-BNP are important parameters alone in post-CPR evaluations and can be included in scoring systems used to predict mortality.

Study Limitations

Limitations of our study include the retrospective design and therefore missing data on patients in the post-CPR period.

Conclusion

In-hospital cardiac arrests and the subsequent support process are considered challenging for clinicians and the healthcare system. It is important to determine the factors affecting survival and good neurological outcomes for the management of the process and clinical care with correct decisions in surviving patients. We think that potassium, NT-pro-BNP and duration of CPR should be considered among these factors. Comprehensive studies are needed to increase the evidence that will shed light on new research.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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